USP Global Public Policy Position

Cannabis and Cannabis-Derived Products:

Advancing Quality and Reducing Patient Harm

Issue

Cannabis and cannabis-derived compounds* are widely used, but their quality is inconsistent. Furthermore, the regulatory oversight for these products varies significantly by locale which poses a risk of harm to patients and consumers.†(1)

Position

To foster consistency in the quality attributes of cannabis and cannabis-derived products to reduce patient and consumer harm, U.S. Pharmacopeia (USP) supports policies that include adherence to a minimum set of national-level, science-based public quality standards‡ irrespective of any regulatory pathway for products containing cannabis and cannabis-derived compounds, including cannabidiol (CBD).

1. **Any cannabis regulatory pathway should require essential elements of oversight and risk assessment.** USP acknowledges the complexity and broad scope of cannabis regulatory issues. This complexity is a reason to integrate standards into the regulatory framework. USP supports concepts that will aid in a regulatory pathway for cannabis and cannabis-derived products that results in quality products such as:
   - Consideration of regulatory pathways, existing or new, for cannabis and cannabis-derived products that **appropriately mitigate associated inherent and quality-related risks and take a harm reduction approach.**
   - **Required registration and listing for all cannabis and cannabis-derived products** which can aid in gaining or increasing visibility into the market.
   - **Oversight and requirements for labeling** to ensure that labels meet established criteria and provide transparency into the ingredients, amounts, and quality of the product.
   - **Oversight of cannabis and cannabis-derived product marketing** to ensure responsible marketing tactics and banning false or misleading claims for cannabis and cannabis-derived products.
   - **Periodic review of the scheduling status of cannabis** to facilitate clinical research, drug development, and understanding of cannabis and cannabis-derived compound pharmacology and toxicology.

2. **A minimum set of uniform public standards for cannabis and cannabis-derived products are necessary and adherence to them must be required.** USP supports the development and use of a minimum set of uniform, national-level public standards for cannabis and cannabis-derived compounds, including CBD, as such public standards are essential to mitigate harm to the patient and consumer. USP urges that products containing cannabis and cannabis-derived compounds adhere to this minimum set of uniform, science-based, public quality standards irrespective of any regulatory pathway. Public standards should, at a minimum, include:
   - **Standardized quality attributes for cannabis and cannabis-derived compounds, including CBD** which can help mitigate public health risks associated with contaminated, substandard, or adulterated products and support sound and reproducible clinical research.
   - **Risk-based limits** to control contaminants including pesticide residues, microbial load, fungal contamination (e.g., aflatoxin), organic solvents, and elemental contaminants (e.g., heavy metals). These limits should be based on toxicological considerations.
   - **Standardized cannabis nomenclature guidelines determined by appropriate analytical tests** to connect the nomenclature of cannabis and related products with specifications for the identification and quantitative determination of critical constituents.

* *Cannabis sativa L.* (cannabis) is a plant that contains over 100 different naturally occurring compounds called "cannabinoids."
Cannabis-derived compounds are compounds occurring naturally in the plant, such as cannabidiol (CBD) and delta-9-tetrahydrocannabinol (THC), that are extracted directly from the plant. Cannabis-derived compounds that may be used in manufacturing human drugs include botanical raw materials (BRMs), extracts, and highly purified substances of botanical origin. Cannabis-derived products contain cannabis-derived compounds.
Cannabis-related compounds are synthetic compounds created in a laboratory and may be used to manufacture drug products. Some may also occur naturally in the plant. Cannabis-related products contain cannabis-related compounds.
Hemp is a legal term defined by the 2018 Agricultural Improvement Act (Farm Bill) and is generally defined as any part of the *Cannabis sativa L.* with a delta-9 THC concentration of not more than 0.3% on a dry weight basis.(1)

† USP acknowledges that laws and regulations that pertain to medicinal or adult recreational use of cannabis in the United States differ between U.S. states and federally. For the purposes of this document, USP does not make a distinction in intended use of the product–adherence to quality standards is necessary for all cannabis and cannabis-related products to protect public health.

‡ For the purpose of this document, USP defines public standards as those developed through a transparent, science–based process allowing for stakeholder input and regular updating to reflect current scientific knowledge. Public standards include scientifically validated testing methods and outline data-driven acceptance criteria to establish specifications for identity, composition, purity, strength, performance attributes, and limits on contaminants or unwanted substances.

- **Standards for labeling** to ensure that labels provide transparency into the ingredients, amounts, and quality of the product.

3. **Additional research is needed to characterize cannabis and cannabis-derived compounds.**
   USP calls for further adequate and well-controlled studies to characterize cannabis and cannabis-derived compounds and supports regulatory and legislative changes necessary to fund and perform well-designed clinical research.

4. **Emerging novel synthesized cannabis-related compounds and their impurities should be monitored and reported.**
   USP recognizes the public health concern associated with novel synthesized cannabis-related compounds, such as delta-8 tetrahydrocannabinol (delta-8 THC), and their analogs, and supports monitoring and reporting of emerging concerns to public health officials for appropriate response.

5. **Promoting safety must be a priority when advancing cannabis policies.**
   Protecting public health and safety must be at the forefront of any discussions related to policies to regulate cannabis and cannabis-derived compounds. As such, USP supports and encourages:

- Efforts to broadly promote the necessity of considering the quality attributes of cannabis and cannabis-derived products among stakeholders.
- Public education programs focusing on the health effects of cannabis.
- Development of health care practitioner and patient and consumer guidelines on the identification of quality cannabis products and their safe use.

Discussion

Cannabis—also referred to as marijuana or marihuana—is a botanical that contains over 100 different naturally occurring compounds known as cannabinoids, the most well-known being delta-9 tetrahydrocannabinol (THC) and CBD, as well as other classes of compounds such as terpenes. Cannabis is among the most commonly used psychoactive drugs in the United States, with an estimated 22 percent of people aged 12 or older (61.9 million people) using it in 2022.(2) According to the United Nations, an estimated 219 million people used cannabis worldwide in 2021, representing 4 percent of the global population.(3) Safety and quality guidelines for cannabis products remain a critical unaddressed issue.

The development and use of public standards and related programs that help ensure the quality, safety, and benefit of medicines, foods, and dietary supplements can improve

global public health. Irrespective of any regulatory pathway for products containing cannabis and cannabis-derived compounds, USP is committed to the development of science-based, public quality standards that include official and validated tests, their analytical procedures, and their acceptance criteria; together these define specifications for identity, strength, performance attributes, and limits for contaminants or unwanted substances.

The standardization of quality attributes is important for cannabis and cannabis-related products due to the wide range of cannabis varieties (chemotypes), the impact of plant material and manufacturing processes on product quality, the remarkable increase in cannabis products available in the global marketplace, and the short- and long-term potential health effects on consumers. The increasing availability and broader sourcing of cannabis products, coupled with the ongoing adoption of initiatives allowing cannabis use across various jurisdictions, increases the risks from contaminated, substandard, or excessively potent products. A minimum set of uniform public standards can help regulators protect public health by providing scientifically validated tests to ensure the identity, constituent composition, and strength of cannabis and cannabis-derived products. Further, regulators can use public standards that set acceptable thresholds for risks from toxic substances, pathogenic microorganisms, and harmful additives to monitor product quality and facilitate consistent manufacturing of products.

Global cannabis regulatory landscape

Cannabis is the third most used psychoactive substance worldwide (after alcohol and tobacco) and is considered the world's most commonly used drug; the number of people who use cannabis has increased by 21 percent over the last decade.(3,4) The legality and regulation of cannabis for medical or recreational use varies by country. According to the United Nations Office on Drugs and Crime, as of 2021, 64 countries had provisions in their national legislation or have developed guidelines allowing the medical use of cannabis or cannabis-derived products for a range of medical conditions.(3)

Global policy measures implemented within regulated markets differ with respect to product standards, labelling and warnings, public education, retail policies, marketing, and price taxation.(5) The European Union, for example, calls for harmonized or standardized laboratory techniques for the characterization of cannabis and cannabis-derived compounds(6) and experts require a comprehensive set of tools to accommodate the growing need for standardization of cannabis and cannabis-derived products.(7)

The cannabis regulatory landscape in the United States is complex

Regulation of cannabis in the United States is complicated. Cannabis plant material containing certain amounts of delta-9 THC is currently classified as Schedule I under the U.S. Controlled Substances Act (CSA) of 1970(8), meaning that such cannabis has no currently accepted medical use in treatment in the United States, a lack of accepted safety for use under medical supervision, and a high potential for abuse.(9) Legally, the term cannabis (or marihuana/marijuana under the CSA) means "all parts of the plant *Cannabis sativa,* whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin."(10) Hemp is excluded from this definition in the CSA since the Agricultural Improvement Act (the 2018 Farm Bill) removed hemp-derived products from Schedule I status under the CSA.(11) The Farm Bill defines hemp as a variety of the cannabis plant containing no more than 0.3 percent delta-9 THC and removed it from Schedule I status under federal law. CBD products that do not meet the statutory definition of hemp continue to be classified as Schedule I under the CSA.

At the state level, trends in laws continue to move along a continuum from legal prohibition, to decriminalization, to the legalization of medical use of cannabis, to cannabis legalized for adult recreational use.(12,13) Each jurisdiction has its own set of laws, regulations, implementation strategies, economic structures, and enforcement tactics. These trends have been shaped by arguments that cannabis is less harmful than alcohol and tobacco and may demonstrate certain health benefits; that arrests and criminal convictions for cannabis possession are disproportionately harmful (including their effect on minoritized populations); and that legalization has the potential to eliminate the illicit market, enable regulation of use (including product potency and purity), reduce prison overcrowding, redistribute law enforcement activities, and raise government revenue.(14)

Several legal challenges, federal agency findings, and federal policy recommendations have attempted to address conflict between federal and state laws and emerging issues on medical or legalized adult use of cannabis.(15-19) Over the

years, presidential administrations and Congress have taken varied approaches to the prioritization of enforcement of marijuana-related activities at the state level. Notably, the U.S. Department of Health and Human Services (HHS)—the U.S. Food and Drug Administration (FDA) with review from the National Institute on Drug Abuse (NIDA)—concluded from an Eight Factor Analysis that cannabis is less harmful than other Schedule I drugs and that there is some evidence of its medical benefits, and recommended cannabis be placed in Schedule III of the CSA.(16,20) In May 2024, the Justice Department, through the Drug Enforcement Agency (DEA), proposed to transfer marijuana from Schedule I to Schedule III, consistent with the recommendation by HHS, noting that if the transfer is finalized, existing marijuana-specific requirements would apply along with any additional controls that might be implemented.(21)

Additionally, the FDA has concluded that existing regulatory frameworks for foods and dietary supplements are not appropriate for CBD and has stated a willingness to work with Congress on a new regulatory pathway that balances access to CBD products with regulatory oversight.(15,22) That notwithstanding, the FDA has expressed concern with CBD and other cannabinoid safety during long-term use, unknown effects from different routes of administration (including nasal, ophthalmic, and inhalation), and an increase in poison control center alerts involving pediatric patients.(15) USP has informed Congressional inquiries into the regulation of cannabis and cannabis-derived products, including CBD.(23)

An FDA drug approval process is available for cannabis and cannabis-derived products

The U.S. Food and Drug Administration (FDA) has approved one cannabis-derived drug product, the CBD oral solution Epidiolex®, and three synthetic cannabis-related drug products, dronabinol (Marinol® and Syndros®) and nabilone (Cesamet®).(24) Additionally, nabiximols (Sativex®), a 1:1 ratio of THC and CBD extracted from specially bred cannabis plants is approved in 20 countries, including Canada, but remains investigational in the United States. The FDA-approved drug products are only available with a prescription from a licensed healthcare provider and the FDA has not approved any other cannabis, cannabis-derived, or CBD products currently available on the market.(24) However, evidence continues to mount that the two primary chemical constituents of cannabis—THC and CBD—could help patients manage anxiety, seizures, chronic pain, and the adverse effects of cancer chemotherapy, among other indications (25,26).

The FDA has provided perspective on cannabis research and development and noted that they continue to observe increasing interest in cannabis and cannabis-derived product development from both academic researchers and commercial product developers(27) and that the FDA's Cannabis Product Committee continues to develop and implement cross-Agency strategy and policy for the regulation of cannabis products.(28) The FDA has stated that the drug development and approval process represents the best way to ensure that safe and effective new medicines are available to patients in need of appropriate medical therapy. This includes drug products that contain cannabis and cannabis-derived compounds.(27,29) Even if DEA transfers marijuana from Schedule I to Schedule III as was outlined in the recent Proposed Rule,(21) any drug containing cannabis would still require FDA approval before legally being marketed and sold in the United States. Furthermore, if cannabis is transferred to Schedule III, it still cannot legally be used recreationally or in food, dietary supplements, tobacco products, or cosmetics.(30)

Cannabis products are evolving

The number of cannabis and cannabis-derived products available commercially is proliferating (31). Additionally, THC concentrations in products sold in global markets have increased from 1970 to 2017.(32) Jurisdictions have put very few limits on the types of products that can be legally sold,

allowing for-profit companies to increase the number and types of products produced and the THC levels in them. Over fifty percent of Americans live in a state where both recreational and medical cannabis are legal, and eight out of ten Americans live in a county with at least one cannabis dispensary.(33)

An expansive retail cannabis marketplace is emerging with a wide array of innovative cannabis products, formulations, and consumption methods. While dried plant material from the cannabis plant still accounts for a large portion of those products used, the increased popularity of food products containing cannabis extracts (edibles), concentrates such as vape oils, or other orally consumed products is reflected in survey data from people who use cannabis.(34) Numerous cannabis product chemotypes with various concentrations of THC and CBD, product formulations, and methods of administration are available to patients and consumers.(35) A typical cannabis retailer will offer plant material, concentrates, tinctures, edibles, vape oils, cannabis-infused beverages, and more.(31) Edibles and other cannabis products, including extracts, topicals, and more also present regulatory challenges.(36-38) The cannabis and cannabis-derived product market is constantly evolving in the type and origin of products, and significant discrepancies between their marketing and their actual ingredients makes these products less transparent for consumers.(39)

Policy solutions are necessary to advance the quality of cannabis and cannabis-derived products and support patient safety

Any cannabis regulatory pathway should require essential elements of oversight and risk assessment

In the absence of a minimum set of uniform standards, when necessary, jurisdictions have adopted their own approaches to oversight of cannabis and cannabis-derived products.§ The application of inconsistent regulatory frameworks and uneven approaches to quality standards can put patients and consumers at risk. Varying amounts of active ingredients in cannabis and cannabis-derived products, as well as any contaminants contained in products can complicate or interfere with care from healthcare practitioners. This variability highlights the urgent need to mitigate the public health risk from cannabis products by introducing a minimum set of uniform, national-level guidelines based on conventional risk assessment methodologies.(42,43) The disparate approaches to oversight of cannabis and cannabis-derived products currently in place create confusion for patients and consumers. **USP acknowledges the complexity and broad scope of cannabis regulatory issues and supports concepts that will aid in a regulatory pathway for cannabis and cannabis-derived products that results in quality products.** These concepts include the following:

- Consideration of regulatory pathways, existing or new, for cannabis and cannabis-derived products that can **appropriately mitigate associated inherent and quality-related risks and take a harm reduction approach should be prioritized.**
- **Required registration and listing for all cannabis and cannabis-derived products** which can aid in gaining or increasing visibility into the market. Required product registration and listing would allow the FDA—as well as patients, consumers, and healthcare practitioners—to have access to basic information about the products being sold, including the ingredients and amounts contained in the product, and a copy of the label. Requiring cannabis and cannabis-derived product manufacturers to register and list all products marketed to the public would support greater transparency in the supply chain and would provide a comprehensive view of the products potentially on the market.
- **Oversight of labeling** is necessary to ensure that labels provide transparency into the ingredients, amounts, and quality of the product. Accurate and informative labeling of cannabis products is an important public health issue. Product labels are considered an essential tool for protecting patients and consumers and enabling informed decision making.(44) Furthermore, missing, or inaccurate labeling of the amount of active cannabinoids may result in harm and/or lack of efficacy.(44)
- **Oversight of cannabis and cannabis-derived product marketing** is necessary to ensure responsible marketing tactics and ban false or misleading claims related to cannabis and cannabis-derived products. Furthermore, studies have examined the sophisticated advertising techniques of emerging cannabis companies, comparing them with well-known lifestyle brands, and highlighting their mass appeal to patients and consumers, including teenagers and children.(45) The use of certain claims

§ As of July 2024 in the United States, twenty-four states, three U.S. territories, and the District of Columbia have legalized recreational use of cannabis. Thirty-eight states, four U.S. territories, and the District of Columbia have legalized medical use of cannabis. Each jurisdiction has unique regulations.(40,41)

in cannabis marketing has also been called into question.(45)

- **Periodic review of the scheduling status of cannabis** should be conducted with goals of facilitating the conduct of clinical research, development of cannabinoid-based medicines, and increasing understanding of cannabis and cannabis-derived compound pharmacology and toxicology.

A minimum set of uniform public standards for cannabis and cannabis-derived products are necessary to prevent harm

Quality standards set forth requirements for nomenclature, describe robust and scientifically valid test methods, and provide information about acceptable test results to define identification, strength or composition, purity, and limits on contaminants for medicines, dietary supplements, and foods. When adopted, these standards allow transparency in how products are tested and assist with identification of adulterated and potentially dangerous products. In addition, the acceptance criteria can be used to standardize the amount of active drug material contained in products so consumers, healthcare practitioners, and patients can understand the products being used.

A recent report from the NASEM, *Cannabis Policy Impacts Public Health and Health Equity,* noted that "[a]ssurance of public health policies in states where cannabis sales are legalized includes consumer protection strategies, but these strategies vary widely in quality control methods and the contaminants tested."(46) Recommendation 4-2 of the report acknowledges the need for the adoption of a uniform set of standards that include quality specifications for cannabis and cannabis-derived products:

"**Recommendation 4-2:** The U.S. Pharmacopeia has established product quality and analytical standards for cannabis inflorescence (flower) and is developing standards for cannabis extracts incorporated into pills and edibles. As these standards are completed, state cannabis regulators should adopt and enforce them to ensure the safety and quality of all legal cannabis products."(46)

A minimum set of national-level public standards for cannabis and cannabis-derived compounds, including CBD, are essential to ensure public trust in products and

help prevent harm to the public. Reports have indicated that analytical tests quantifying the amount of THC in cannabis products can yield inconsistent results because of insufficient standardization of sample preparation and testing methods(47,48); even those in the cannabis industry have been advocating for greater uniformity in the methodologies being used for cannabis testing(49) and the issue of inconsistent laboratory testing is consistently highlighted as a concern for the industry.(50) Because of the numerous pharmacologically active compounds in cannabis and cannabis-derived products currently available, validated, and standardized analytical testing methods are critical to ensure consistency and patient safety.

USP supports the development and use of a minimum set of uniform, national-level public standards for cannabis and cannabis-derived compounds, including CBD, as such public standards are essential to help prevent harm to patients and consumers. Public standards should, at a minimum, include standardized cannabis quality attributes, a single set of cannabis contaminant limits, standardized cannabis nomenclature determined by appropriate analytical tests, and standards for labeling.

Cannabis and cannabis-derived product quality attributes

Ensuring the quality of cannabis and cannabis-derived products requires appropriate sampling procedures and a suite of tests, analytical procedures, and acceptance

criteria to define the identity, content of constituents, and limits on contaminants. A Cannabis Expert Panel formed by USP evaluated specifications necessary to define key cannabis quality attributes and determined that these specifications should differentiate between cannabis plant types (chemotypes): THC-dominant chemotype; intermediate chemotype with both THC and CBD; and CBD-dominant chemotype. Cannabis plants in each of these chemotypes may be further subcategorized based on the content of other cannabinoids and/or terpene profiles. Because the effects of the cannabis article depend on its chemical composition, the fit-for-purpose validated analytical methods needed to quantitatively estimate the constituents have been developed and outlined by the Expert Panel.(51) **Standardized cannabis and cannabis-derived product quality attributes can help mitigate public health risks associated with contaminated, substandard, or adulterated products and support sound and reproducible clinical research.**

Cannabis contaminant limits

During cultivation and processing, cannabis and cannabis-derived products can be contaminated with potentially harmful substances.(43,52,53) Contaminants, including pesticide residues, microbial load, aflatoxin levels, organic solvents, and elemental contaminants, present significant risks to the quality and safety of cannabis and cannabis-derived products. Research has reported inconsistency in cannabis-borne contaminant regulation, greater risk of contaminant exposure from cannabis and cannabis-derived products, and a need for a unified, single set of regulatory guidelines to mitigate the public health risk of cannabis contamination at a national level that is based on scientific data.(43) Risk-based limits for contaminants should be based on the assessment of available information from multiple sources. Tests and assays contained in public quality standards provide analytical methods and acceptance criteria to control contaminants and provide guidelines for quality assurance. **A single set of cannabis contaminant limits, based on toxicological considerations, is necessary to control contaminants including pesticide residues, microbial load, aflatoxin levels, organic solvents, and elemental contaminants.**

Cannabis nomenclature

Botanical quality is impacted by several variables, including plant genetics, cultivation, collection, and post-harvest conditions. Cannabis nomenclature is complex; ongoing debate persists about the number of species, and there is no consensus on a unified cannabis taxonomy classification system.(54) Even within the same chemotype and growing conditions, there could be considerable variation in cannabinoid content, which can present a challenge to maintaining consistent quality across products. Recent research notes that composition data are reported inconsistently due to an insufficient standardization of sample preparation and testing methods, thus likely leading to erroneous product information.(47) Establishing and standardizing accurate descriptions, appropriate nomenclature, and validated analytical testing of cannabinoid content for regulatory purposes is critical for cannabis and cannabis-derived compounds and could provide information on the quality attributes and materials used in the manufacture of products. This information can also help manufacturers with Current Good Manufacturing Practices (CGMP) and other manufacturing requirements. **Standardized cannabis nomenclature guidelines determined by appropriate analytical tests is necessary to connect the nomenclature of cannabis and cannabis-derived products and the specifications required for identifying and quantitatively measuring their critical constituents.**

Labeling standards

Research shows cannabis and cannabis-derived products on the market can be inaccurately labeled and may contain

more or less THC than is indicated on the label. Inaccurate labels present consumer safety issues.(55) As the cannabis and cannabis-derived product market continues to grow, its packaging is critically important. Considerations about cannabis and cannabis-derived product packaging include the use of both implicit and explicit claims, appeal to youth, and overall perception by consumers.(56) **Standards for labeling are necessary to ensure that labels provide transparency into the ingredients, amounts, and quality of the product.**

All cannabis and cannabis-derived products should adhere to public quality standards

In the absence of a minimum set of national standards, when necessary, states have adopted their own approaches to oversight of cannabis and cannabis-derived products. The application of inconsistent regulatory frameworks and uneven approaches to quality standards can put consumers at risk. Establishing and standardizing accurate descriptions, appropriate nomenclature, and validated analytical testing of cannabinoid content for regulatory purposes is critical for cannabis and cannabis-derived compounds and could provide information on the quality attributes and materials used in the manufacture of products. USP works with independent experts from industry, academia, regulation, and healthcare in a collaborative approach to standards development that helps ensure emerging technologies and evolving public health needs are addressed, including for cannabis and cannabis-derived compounds. **USP urges that products containing cannabis and cannabis-derived compounds, including CBD, should adhere to a minimum set of uniform, science-based, public quality standards irrespective of any regulatory pathway.**

Additional research is needed to characterize cannabis and cannabis-derived compounds

While the health effects of cannabis and cannabis-derived products have been documented,(26) ongoing research aims to enhance the consistency of cannabinoid analyses,(47) explore daily intake limits,(57) better understand the potential harms and benefits of cannabis and cannabis-derived products, and more.(58) As of March 2024, there were at least 245 active clinical trials exploring the positive and negative medical effects of cannabis.(59)

The Medical Marijuana and Cannabidiol Research Expansion Act (MMCREA), signed into law in 2022, is the first standalone marijuana-related bill approved by both chambers of the United States Congress(60) and was designed to facilitate medical research on cannabis, accelerate the development

of trusted preclinical and clinical principles based on scientific data, inform lawmakers, and protect public health.(61) The Act establishes a new registration process for researching cannabis and cannabis-derived products, requires HHS to investigate the medical utility of cannabis and barriers to conducting research, requires the U.S. Attorney General to conduct an annual review to ensure that cannabis is being adequately produced for research purposes, protects healthcare providers who discuss the harms and benefits of using cannabis and cannabis-derived products, and creates a mechanism for FDA approval of cannabis and cannabis-derived drugs. A recent report from HHS required under MMCREA details several barriers currently facing researchers investigating cannabis and cannabis-derived products, including confusion related to federal definitions for cannabis and hemp, access to products for research purposes, and challenges related to regulations associated with the study of a Schedule I drug.(62)

The FDA understands and has acknowledged the increasing interest in the potential utility of cannabis and cannabis-derived compounds for a variety of medical conditions, as well as research on their potential adverse health effects.(24) Additionally, a recent FDA Guidance, *Cannabis and Cannabis-Derived Compounds: Quality Considerations for Clinical Research Guidance for Industry,* outlines FDA's current thinking on several topics relevant to clinical research related to the development of human drugs containing cannabis or cannabis-derived compounds.(63)

Various groups have highlighted additional areas of research necessary to better understand the harms and benefits associated with cannabis and cannabis-derived products, which is crucial for informing regulations and policies, as well as some of the challenges associated with conducting this work.(64) As THC concentrations increase and the type and number of cannabis and cannabis-derived products grows, the need for additional research to better characterize them also increases. A significant impediment for researchers in the United States is the difficulty in obtaining high-potency products in clinical studies.(31) Furthermore, increased use of cannabis products in patients with co-morbid conditions has raised questions about potential drug-drug interactions between cannabis and other prescribed medications.(65,66) Another important challenge facing clinical studies involving cannabis and cannabis-derived products is a lack of standardization of dosing. The National Institute on Drug Abuse (NIDA) strongly supports the need for a standardized measure to facilitate research on cannabis and cannabis-derived products and to enable comparison of products.(67)

USP calls for further adequate and well-controlled studies to characterize cannabis and cannabis-derived compounds and supports the regulatory and legislative changes necessary to fund and perform well-designed clinical research related to cannabis and cannabis-derived compounds.

Emerging novel synthesized cannabis-related compounds and their impurities are a public health threat

The emergence of minor cannabinoids and synthetic cannabinoid analogs in the marketplace is a public health threat. Delta-8 THC, a psychoactive substance, is one of the hundreds of cannabinoids produced naturally by the cannabis plant. Delta-8 THC is not found in significant amounts in the cannabis plant but has recently been found in concentrated amounts in products available for purchase in retail outlets.(68) To obtain the concentrations of delta-8 THC claimed in the marketplace, potentially harmful chemicals are used to manufacture the compound using hemp-derived CBD. Delta-8 THC is associated with adverse health outcomes, little research is available evaluating the pharmacology and toxicology of the compound, and a recent study noted a significant increase in exposure to delta-8 THC reported to U.S. poison centers.(69) The FDA has warned that delta-8 THC has serious health risks(70) and has published a series of warning letters to companies selling delta-8 THC products noting that the FDA has received adverse event reports involving delta-8 THC products; delta-8 THC has psychoactive and intoxicating effects; the FDA is concerned about the processes used to create the concentrations of delta-8 THC claimed in the marketplace; and the FDA is concerned about delta-8 THC products that children may consume, as some packaging and labeling may mimic the appearance of well-known items that appeal to children.(71,72)

Since the proliferation of delta-8 THC, other THC isomers (e.g., delta-10 THC, delta-8-THC-O-acetate, hexahydrocannabinol, and tetrahydrocannabiphorol) are emerging in the marketplace with no safety or toxicity data in an attempt to exploit a loophole in U.S. regulations for hemp that specifically listed limits for delta-9 THC.(73) Products containing these THC isomers (commonly referred to as "intoxicating hemp products") are of serious concern for state regulators.(74) Public quality standards and validated analytical methods are important tools to detect and control for the presence of these adulterants in

products and highlight the public health concern associated with them.(75) **USP supports monitoring and reporting of emerging concerns from novel synthesized cannabis-related compounds, such as delta-8 THC, and their analogs to public health officials for appropriate response. Because these compounds are a public health concern, USP urges that they be treated as adulterants in cannabis products until their safety and efficacy has been established.**

Promoting public health and safety must be a priority when advancing cannabis policies

Support for the legalization of cannabis and cannabis-derived products has increased over the past twenty years.(33) As conversations continue about the benefits and harms associated with cannabis and cannabis-derived product use, it is imperative to leverage an evidence-based public health approach when advancing policies to minimize risk to users. Public health organizations continue to the call for efforts to minimize harm to the public and the use of an evidence-based public health approach to addressing cannabis and cannabis-derived product use; the protection of children, vulnerable, and marginalized populations; informing individuals about the health effects associated with chronic cannabis use; continued, rigorous research to better understand the pharmacology and toxicology of cannabis and cannabis-derived products; the better understanding cannabis and cannabis-derived products online sales and associated risks; and monitoring patterns of cannabis use and prevalence of cannabis use disorder.(38,76-78)

Healthcare provider organizations are closely monitoring the public health impacts of cannabis and cannabis-derived products and urge evidence-based policymaking and updated public health frameworks to minimize harms potentially associated with cannabis use.(78,79) Furthermore, guidelines on the identification of quality cannabis products and their safe use could benefit both healthcare providers and consumers; studies have shown that guidance can help healthcare practitioners engage in conversations with patients to guide individualized patient care decisions about minimizing risk and considering quality when choosing cannabis and cannabis-derived products.(80) Healthcare providers should be equipped with educational resources to effectively communicate with patients about their cannabis use. Many patients, especially those using cannabis recreationally, may not consider it necessary to disclose their consumption to their doctors, or they may fear stigma or judgment. This lack of open communication can be problematic, as cannabis use can potentially impact the effectiveness and safety of medical treatments. By providing healthcare professionals with the tools and knowledge to approach the topic of cannabis use with sensitivity and understanding, patients may feel more comfortable discussing their consumption habits, leading to better-informed treatment decisions and improved patient outcomes.

Consideration of the quality attributes of cannabis and cannabis-derived products should be widely promoted, especially as the availability of novel types of cannabis and cannabis-derived products grows. For example, vaping cannabis is increasing(81) and while most products are labeled as to content, the quality control of manufacturers and the relative safety of vaping products is uncertain.(75,82) The issues associated with testing accuracy, labeling transparency, and marketing tactics should be emphasized to all patients and consumers, and the importance of quality considerations should be promoted among all populations. Further, cannabis advertising regulations vary greatly and have little consistency across U.S. states. This lack of consistent marketing guidelines could expose youth and vulnerable populations to cannabis advertisements; more widespread or federal guidance is needed to limit risk to these populations.(83)

Protecting public health and minimizing harm to the public must be at the forefront of any discussions related to policies to regulate cannabis and cannabis-derived compounds. Investment in and availability of quality products, guidance on identifying quality products, and prevention education programs can minimize public harm. As such, **USP supports and encourages efforts to promote the necessity of considering the quality attributes of cannabis and cannabis-derived products; public education programs focusing on the health effects of cannabis; and development of health care practitioner and patient and consumer guidelines on the identification of quality cannabis products and their safe use.**

About USP

The United States Pharmacopeia (USP) is an independent, scientific, nonprofit organization devoted to developing and formalizing science-based quality standards and related programs for medicines, dietary supplements, and foods based on volunteer expert advice from the medical and scientific community. USP publishes two legally recognized

Official Compendia of the United States, combined into a single publication, the *United States Pharmacopeia-National Formulary (USP-NF)*. USP also publishes a compendium of food ingredient standards in the *Food Chemicals Codex* (FCC). One of USP's areas of expertise and focus is the development of quality standards for botanical ingredients, including analytical testing methods and requirements to help ensure their identity, purity, strength, and limits on contaminants. Find USP resources for cannabis here.

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